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Original Article

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Neuropsychiatric Manifestations of Patients with Chronic Kidney Disease in Southeast Nigeria

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ABSTRACT

Objective: Chronic kidney disease is associated with several physical and psychosocial burdens which significantly impact the patient's quality of life and functionality. This psychological impact of chronic kidney disease is heightened in developing countries with lots of compounding factors including poverty, poor infrastructure including poor health facilities, and non-existent/poorly implemented health policies.

Methods: This is a cross-sectional analytical study of patients attending Enugu State University of Science and Technology (ESUT) Teaching Hospital Parklane, Enugu, from November 1, 2018, to April 30, 2019. Consecutive patients presenting to the renal unit of the hospital who met the inclusion criteria were recruited for the study from Medical out patient (MOP) and renal clinics. The clinical details including biodata and blood samples were collected from the patient. The estimated glomerular filtration rate was calculated using modification of diet in kidney diseases (MDKD) formula.

Results: A total of 153 patients were recruited, 63.8% were males with a mean age of 51.4 ± 15.5 years. Most of the patients (90.9%) were in chronic kidney disease stages 3-5; 90.2% had comorbidities and 56.2% were on hemodialysis; however, only 14% adhere to the hemodialysis prescription. The prevalence of neuropsychiatric manifestation was 71.2%, and depression and anxiety disorder were the most common with the prevalence of 58.2% and 20.3%, respectively. Other neuropsychiatric manifestations in this study include post-traumatic disorder, bipolar disorder, schizophrenia, obsessive–compulsive disorder, suicide ideation, and hypomania. Occupation, diabetes mellitus, and late stages of chronic kidney disease were predictors of neuropsychiatric disorder in chronic kidney disease patients.

Conclusion: Neuropsychiatric disorder of various types is a common presentation in patients with chronic kidney disease. Occupation, diabetes mellitus, and late stages of chronic kidney disease are risk factors for the development of neuropsychiatric disorder in chronic kidney disease patients.

Keywords: Neuropsychiatric, chronic kidney disease, hemodialysis, manifestations

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INTRODUCTION

Patients with chronic kidney disease (CKD) have multiple losses that significantly impact their quality of life and functionality. They usually present with many physical and neuropsychiatric manifestations in the course of the illness. These manifestations are associated with biochemical, hematological, and neurohumoral abnormalities that are caused by kidney dysfunctions.[1]

Neuropsychiatric disorder has been reported as a common presentation in patients at various stages of chronic kidney disease.[2,3] Fatigue, drowsiness, and inability to concentrate for long periods are among the early symptoms of patients with CKD. These features adversely influence the morbidity and mortality associated with chronic kidney disease. Hospitalizations due to neuropsychiatric disorders are 1.5-3 times more common

among patients with CKD than individuals with other chronic diseases.[4]

Chronic kidney disease is a constant psychological process for patients and their families so as to acknowledge their new image and to be conformed to the new state of their treatment.[5] It is an independent risk factor for the development of neuropsychiatric disorders and it has been reported that there is a decline in cognitive function for every 10-15mL/min/1.73 m^2 reduction in glomerular filtration rate (GFR).[2,6] The need for renal replacement therapy, especially hemodialysis, has been associated with higher prevalence and morbidity of neuropsychiatric disorder in CKD patients.[7]

The management of CKD is complex and expensive with subsequent financial and psychosocial burdens on the patients, families/caregivers, and the communities. These include dietary restrictions and lifestyle modifications thus distorting the already established patient's mode of living and wellbeing. Chronic kidney diseases are often associated with many comorbidities requiring multiple drug regimens, thus exposing the patients to many adverse effects and toxicities which may include neuropsychiatric disorder.[8,9] Diagnoses of CKD are initially accompanied by denial and subsequently acknowledgment of their state and modalities of intervention which places a psychological burden on patients and caregivers.[10] In most developing countries including Nigeria, the management of CKD is borne solely by the patients and relatives with its antecedent financial and psychological liabilities.

The interactions between kidney and brain are complex and multifaceted, thus justifying the significant neuropsychiatric comorbidity observed in patients with CKD. The actual pathogenetic pathways are not known; however, some hypothesis suggests that microvascular injuries, accumulation of toxins, and hemodynamic changes in the brain are the mechanisms of neuropsychiatric diseases in CKD.[11] Uremic toxins released as a result of CKD are thought to directly contribute to brain damage and consequent neuropsychiatric disorders.

Multidisciplinary approach involving the primary care physicians, nephrologists, and psychiatrists in the management of patients with CKD will be beneficial to them. Also, screening for neuropsychiatric disorder in CKD patients will lead to early detection and prompt intervention with an expected better outcome. There are few studies of neuropsychiatric manifestation in patients with CKD, and none has been reported in southeast Nigeria.

The objective of this study is to assess the neuropsychiatric manifestations of patients with CKD in a teaching hospital in southeast Nigeria.

MAIN POINTS

- The majority of patients with chronic kidney disease (CKD) develop neuropsychiatric manifestation.
- Neuropsychiatric manifestation is more prevalent in patients with CKD stages 3, 4, and 5.
- Depression and anxiety were the most common neuropsychiatric disorder in CKD patients.
- Risk factors for the development of neuropsychiatric disorder in these CKD patients were occupation, diabetes mellitus, and late stages of CKD.

METHODS

This is a hospital-based cross-sectional analytical study of patients with chronic kidney disease who presented to the renal unit of ESUT Teaching Hospital, Parklane, Enugu, from November 1, 2018, to April 30, 2019. The hospital attends to patients from all the South Eastern states of Enugu, Anambra, Ebonyi, Abia, and Imo. It is a 350 bedded tertiary health institution with various specialty and subspecialty departments. The study was approved by the Ethics Committee of ESUT Teaching Hospital, Parklane, Enugu Nigeria (Approval Date: October 9, 2018; Approval Number: ESUTHP/5/EC/032/18).

Inclusion Criteria

- patients with chronic kidney disease presenting to the hospital during the study period;
- patients who have given consent for the study;
- adult patients who are 18 years and above.

Exclusion Criteria

- patients less than 18 years old;
- patients with a past history of psychiatric illness;
- patients with psychiatric illness predating CKD;
- unconscious or severely ill patients;
- patients that declined consent for the study.

Procedure

Consecutive patients with chronic kidney disease who met the inclusion and exclusion criteria were recruited for the study from the medical outpatient, renal clinic, medical wards, and hemodialysis unit. The details of the study were explained to the patients and informed consent was obtained from each patient. The biodata including age, sex, occupation, religion, and levels of education was documented. Also, the patients were assessed clinically and the parameters obtained were recorded. The specimen was collected for the assessment of packed cell volume (PCV), serum creatinine, and serum urea, and the results obtained were documented. The estimated GFR (eGFR) of each patient was calculated using the modification of diet in renal disease (4 variables) and the value obtained was documented. The patients were assessed for neuropsychiatric disorders using the module of MINI International Neuropsychiatric Inventory which is a structured diagnostic interview questionnaire. This was administered to each of the patients and their responses were documented.

Statistical Analysis

The data obtained were analyzed using SPSS version 22 (IBM Corp., Armonk, NY, USA). The variables were expressed as percentages, median, interquartile range, means, and standard deviation using descriptive statistics. Pearson's correlation test was used to test for association probability between the various participants` characteristics and having neuropsychiatric disorder, while the predictors of neuropsychiatric disorders among chronic kidney disease patients were determined with binomial logistic regression test. A *P*-value of <.05 was taken to be statistically significant and the CI was at 95%.

RESULTS

Biodata

A total of 153 patients were recruited during the period of the study. The majority of the patients were males (63.8%) with male to female ratio of 1.8 : 1. The mean age was 51.4 ± 15.5 years with a range of 19-90 years and median of 52 years. Most of the patients were Ibos (96.7%), Christians (96.7%), civil servants (42.5%), and had secondary education (47.1%). The details of the biodata are shown in Table 1.

Table 1. Demographic Characteristics

Characteristics	Male (%)	Female (%)	Total (%)	*P*
Age distribution (years)				
<30	9 (5.9)	5 (3.3)	14 (9.2)	.23
30-39	15 (9.8)	13 (8.5)	28 (18.3)	
40-49	13 (8.5)	8 (5.2)	21 (13.7)	
50-59	22 (14.4)	20 (13.1)	42 (27.5)	
60-69	23 (15)	7 (4.6)	30 (19.6)	
≥70	15 (9.8)	3 (2)	18 (11.8)	
Total	97 (63.8)	56 (36.2)	153 (100)	
Education				.99
Primary, n (%)	16 (10.5)	9 (5.9)	25 (16.4)	
Secondary, n (%)	35 (22.9)	21 (13.7)	56 (36.6)	
Tertiary, n (%)	46 (30.1)	26 (17.0)	72 (47.1)	
Occupation				.01
Civil servant, n (%)	41 (26.8)	24 (15.7)	65 (42.5)	
Business, n (%)	27 (17.6)	26 (17.0)	53 (34.6)	
Farming, n (%)	9 (5.9)	5 (3.3)	14 (9.0)	
Artisan, n (%)	7 (4.6)	1 (0.7)	8 (5.3)	
Unemployed, n (%)	13 (8.5)	0 (0.0)	13 (8.5)	
Religion				.14
Christian	92 (60.1)	56 (36.6)	148 (96.7)	
Muslim	5 (3.3)	0 (0.0)	5 (3.3)	
Tribe				.14
Ibo	92 (60.1)	56 (36.6)	148 (96.7)	
Hausa	5 (3.3)	0 (0.0)	5 (3.3)	

Clinical Parameters

Hypertensive nephrosclerosis, diabetic nephropathy, and chronic glomerulonephritis were the commonest causes of chronic kidney disease in this study. Seventy-nine (51.6%) patients were in the end stage of kidney disease. Most of the patients (90.2%) had comorbidities, 81% of the patients were hypertensives, and 37.9% had diabetes mellitus. The details of the clinical parameters are shown in Table 2.

Laboratory and Treatment Parameters

The mean PCV was 27.8 ± 12.7%; however, 76.5% and 57.5% had PCV less than 33% and 30%, respectively.

About 51%, 40.5%, and 78.5% received blood transfusion, erythropoietin, and parenteral iron, respectively. Only 6.5% adhered to the erythropoietin prescription.

The median serum urea, creatinine, and eGFR were 42.8 (4.7-200) mg/dL, 4.12 (0.4-22.9) mg/dL, and 14(2-306) mL/min/1.73 m^2, respectively.

Eighty-six (56.2%) patients had hemodialysis during the study period; however, only 14% of them were regular on the dialysis as prescribed. The mean duration of hemodialysis was 6.69 ± 6.09 weeks. None was on peritoneal dialysis or had kidney transplant and the details are shown in Table 3.

Neuropsychiatric Manifestations

One hundred nine (71.2%) patients had neuropsychiatric manifestations with 45.1% being males. The majority of the patients with neuropsychiatric manifestations were in late stages (stages 3-5) of CKD. The detailed distribution of neuropsychiatric manifestation according to the stages of CKD is shown in Figure 1.

Depression and anxiety were diagnosed in 58.2% and 20.3% of patients, respectively. There was no significant difference in the gender of those with neuropsychiatric manifestations. The details are as shown in Table 4.

Correlations

Occupation, diabetes mellitus, PCV, and eGFR had a significant negative correlation with neuropsychiatric manifestation, while hypertension, urea, creatinine, use of iron, erythropoietin, blood transfusion, and dialysis had a significant positive correlation with neuropsychiatric manifestation. The details are as shown in Table 5.

Table 2. Clinical Parameters

Characteristics	n (%)
Causes of CKD	
Hypertensive nephrosclerosis	63 (41.2)
Diabetic nephropathy	39 (25.5)
Chronic glomerulonephritis	26 (17)
HIVAN	9 (5.9)
Post AKI	8 (5.2)
Toxic nephropathy	4 (2.6)
Obstructive nephropathy	3 (2.0)
Unknown	1 (0.7)
Stages of CKD	
Stage 1	7 (4.6)
Stage 2	7 (4.6)
Stage 3	31 (20.3)
Stage 4	29 (19.0)
Stage 5	79 (51.6)
Hypertension	124 (81)
Diabetes mellitus	58 (37.9)
Comorbidities	138 (90.2)

CKD, chronic kidney disease; HVAN, HIV associated nephropathy; AKI, acute kidney injury.

Table 3. Laboratory and Treatment Parameters

Parameter	n (%)
Treatment	
Hemodialysis	86 (56.2)
Regular[a]	12 (14.0)
EPO	62 (40.5)
Regular[a]	10 (6.5)
Blood transfusion	78 (51.0)
Iron (parenteral)	120 (78.5)
Laboratory	
PCV (mean ± SD) %	27.7 ± 6.8
SUN (median (IQR)) mg/dL	42.8 (4.7-200)
SCr (median (IQR) mg/dL	4.12 (0.4-22.9) mg/dL
eGFR (median (IQR) mL/min/1.73 m^2	14 (2-306)

[a]Adhere to prescription. EPO, erythropoietin; PCV, packed cell volume; SUN, serum urea; SCr, serum creatinine; eGFR, estimated glomerular filtration rate; IQR, interquartile range; SD, standard deviation.

Predictors of Neuropsychiatric Manifestations

On binominal logistic regression, occupation (CI = 0.460-0.949), diabetes mellitus (CI = 0.064-0.601), and eGFR (CI = 0.952-0.995) were significant predictors of neuropsychiatric manifestation in these patients. The details are shown in Table 6.

DISCUSSION

Chronic kidney disease in resource-poor nations has been reported to be more prevalent in the economically active group of the population, especially in the young adults and middle age group.[12] This is consistent with the findings of this study where about 68% of the patients were less than 60 years and mainly civil servants. The management of CKD is expensive, and unlike the case in developed countries where government and its agencies subsidize the cost of treatment, patients in most developing countries including Nigeria solely finance the cost of their treatment. Thus CKD and its management place a great physical, financial, and psychological burden on the patients, relatives, and community with the affection of the economically active group of the population.[10]

Patients with CKD usually develop significant clinical manifestations in the later stages (stages 4 and 5) of the disease and this is usually when most present to the hospital. However, this group constitutes a smaller proportion of the CKD patient population and is usually described as the tip of the iceberg.[13] Unfortunately, in most resource-poor nations as in this study, patients in the late stages of CKD constitute the majority of patients diagnosed with CKD. They usually present with multiple complications and comorbidities. In this study, 70.6% of the patient population were either in stage 4 or 5 CKD with the majority of them presenting with complications and comorbidities—81% with hypertension, 38% with diabetes mellitus, and 76.4% with anemia (PCV less than 33% as recommended by Kidney Disease Improving Global Outcome).[14] Most of the patients received treatment for anemia including blood transfusion in 51.0%, parenteral iron in 78.5%, and erythropoietin in 40.6%; however, less than 6.5% were regular with erythropoietin. Adejumo et al[15] reported that 85.6% of patients presenting at their center were in CKD stage 5 with the majority of them being anemic, hypertensive, and requiring urgent hemodialysis. These late presentations of patients with CKD are attributed to poverty, ignorance, and lack of adequate health care facilities to detect CKD at earlier stages. Hypertensive nephrosclerosis, diabetic nephropathy, and chronic glomerulonephritis were the commonest causes of CKD in this study, which is consistent with the report of previous studies in Nigeria.[12,15,16]

Addison in his classic monograph in 1868 reported that patients with renal failure present with “a dullness of the intellect, sluggishness of manner, drowsiness going on to quiet stupor, and coma.”[17] Since then, it has been noted that CKD is an independent risk factor for the development of neuropsychiatric

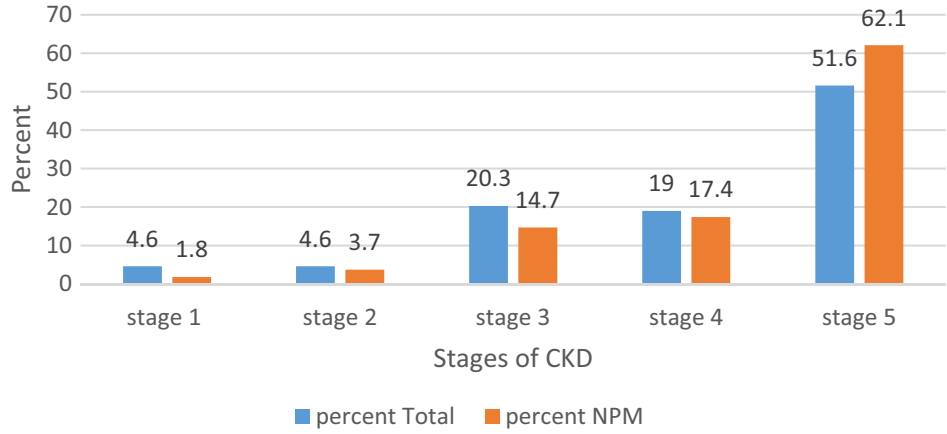

Figure 1. Distribution of Neuropsychiatric manifestations (NPM) according to the stages of CKD. CKD, chronic kidney disease.

Table 4. Gender Distribution of Neuropsychiatric Manifestations

Characteristics	Male	Female	Total	*P*
Depressive disorder	54 (35.3)	35 (22.9)	89 (58.2)	.51
Suicide	2 (1.3)	4 (2.6)	6 (3.9)	.12
Obsessive–compulsive disorder	7 (4.6)	3 (2.0)	10 (6.6)	.65
Post-traumatic stress disorder	14 (9.2)	6 (3.9)	20 (13.1)	.51
Anxiety disorders	18 (11.8)	13 (8.5)	31 (20.3)	.63
Schizophrenia	2 (1.3)	0 (0.0)	2 (1.3)	.28
Bipolar mania, n (%)	2 (1.3)	0 (0.0)	2 (1.3)	.28
Depression with psychosis, n (%)	9 (5.9)	2 (1.3)	11 (7.2)	.19
Hypomania	0 (0)	1 (0.7)	1 (0.7)	.17

Table 5. Pearson's Correlations of Neuropsychiatric Manifestation with Some Clinical and Treatment Parameters in CKD Patients

Parameter	*R*	*P*
Age	−0.03	.22
Sex	0.00	.15
Education	0.15	.09
Occupation	−0.18	.01
Hypertension	0.17	.04
Diabetes mellitus	−0.25	.01
Comorbidities	0.08	.38
PCV (%)	−0.29	.02
Urea (mmol/L)	0.21	.01
Creatinine (umol/L)	0.36	.01
eGFR (mL/min/1.73 m^2)	−0.36	.01
Parenteral iron	0.26	.03
Erythropoietin	0.32	.04
Blood transfusion	0.30	.01
Dialysis	0.40	.01

CKD, chronic kidney disease; PCV, packed cell volume; eGFR, estimated glomerular filtration rate.

disorders.[5,6] In this study, 109 patients constituting 71.2% of the study population presented with various neuropsychiatric manifestation. This is consistent with the report of the prevalence of 70% by Elhadad et al[18], in a study of psychiatric comorbidity in CKD patients undergoing hemodialysis. However, this is at variance with the findings of many other studies that reported a lower prevalence of neuropsychiatric comorbidities in CKD patients.[2,3,19,20] These discrepancies may have been associated with the current socioeconomic status of the studied population, the instrument used to diagnose neuropsychiatric disorder, and sample size.

Depressive disorder was the commonest neuropsychiatric manifestation in this study with a prevalence of 58.2%, which is consistent with other studies that had variously reported depression as the commonest neuropsychiatric presentation in CKD patients. The prevalence of depression in CKD patients in Nigeria had been previously reported to be 22%-35%[19-21] by previous studies. Many somatic symptoms of CKD including fatigue, anorexia, weight, and sleep disorders may be misdiagnosed as depression depending on the diagnostic tool. Furthermore, the prevailing economic state of the country may have influenced the higher prevalence of depression in this study.

Chronic kidney disease patients have been reported to be more prone to develop anxiety and other anxiety-related neuropsychiatric disorder.[22] It is the second most common neuropsychiatric manifestation in this study with a prevalence of 20.1%.

Table 6. Predictors of Neuropsychiatric Manifestations

Variable	*B*	*P*	95% CI
Occupation	−0.41	.025	0.460 - 0.949
Cause of CKD	−0.11	.504	0.661-1.226
HTN	0.65	.244	0.641-5.726
Diabetes mellitus	−1.63	.004	0.064-0.601
PCV (%)	−0.004	.921	0.912-1.087
Urea (mmol/L)	−0.004	.858	0.958-1.036
Creatinine (umol/L)	−0.001	.154	0.997-1.000
eGFR (mL/min/1.73 m^2)	−0.027	.015	0.952-0.995
Parenteral iron	0.42	.46	0.498-4.625
Erythropoietin	0.89	.22	0.593-9.919
Blood transfusion	−0.53	.48	0.133-2.581
Dialysis	1.01	.14	0.712-10.653

CKD, chronic kidney disease; PCV, packed cell volume; eGFR, estimated glomerular filtration rate.

Previous studies have reported variable prevalence of anxiety in CKD patients, ranging from 0% to 52 %.[23,24] Anxiety symptoms may be associated with poor clinical and psychological outcomes like poor health-related quality of life, hospitalization, and mortality.

Chronic kidney disease patients in this study also presented with other neuropsychiatric manifestations including post-traumatic stress disorder (PTSD) in 13.1%, bipolar disorder in 8.5%, obsessive–compulsive disorder in 6.6%, suicidal ideation in 3.9%, schizophrenia in 1.3%, and hypomania in 0.7%. Edmondson et al[25] reported a higher prevalence of PTSD (24%) among patients with End stage kidney disease (ESKD). Other studies have reported varying prevalence of neuropsychiatric disorders in CKD patients depending on the distribution of the studied population, the severity of kidney disease, and the diagnostic tools used for this study.[19,26-29]

Neuropsychiatric manifestation was found to have a significant correlation with decreasing kidney function with most of the patients (94.5%) in stages 3-5 CKD. Also, about 86% of patients in stage 5 CKD as compared to only 29% of those in stage 1 CKD had neuropsychiatric disorder. Furthermore, late stages of CKD are a predictor and a risk factor for the development of neuropsychiatric disorder in this study and this is consistent with a report of other studies.[3,4] Hemodialysis, a very important therapeutic procedure in the management of patients with late stages of CKD, also impacts marked social, economic, and psychological burden on the patients,[19,30] and this is also reflected in this study as hemodialysis has a significant correlation with neuropsychiatric manifestation.

Occupation, hypertension, diabetes mellitus, and anemia are other factors found to have a significant relationship with the development of neuropsychiatric disorder in the study. However, on multiple regressions, only occupation and diabetes mellitus in addition to decreasing kidney function were significant and thus are predictors of neuropsychiatric disorder. Ayanda et al[19] reported a high prevalence of psychiatric disorders in CKD patients with comorbidity and on hemodialysis. Also, other factors reported to be associated with the development of neuropsychiatric disorders include anemia, hyponatremia, hypertension, and some antihypertensive drug including alpha methyldopa.[11,18]

This study has some limitations including the cross-sectional nature which does not include intervention/outcome as variables, being hospital-based, and thus did not include many with early stages of CKD. However, the study was able to highlight the various types of neuropsychiatric manifestation in patients with different stages of CKD and some of the risk factors.

CONCLUSION

More than 70% of CKD patients studied presented with neuropsychiatric manifestation, and depression is the most prevalent presentation with a prevalence of 58.2%. Occupation, diabetes mellitus, and late stages of CKD were predictors of neuropsychiatric manifestation in the study. Thus, there is a need for screening for neuropsychiatric manifestation on CKD patients at presentation to ensure early detection and intervention. This thus highlights the need for a multidisciplinary approach that should include psychiatrists in the management of patients with CKD.

Ethics Committee Approval: Ethics committee approval was received for this study from the Ethics Committee of ESUT Teaching Hospital, Parklane, Enugu Nigeria (Approval Date: October 9, 2018; Approval Number: ESUTHP/5/EC/032/18).

Informed Consent: Informed consent was obtained from the patients who participated in this study.

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